

Attorney Docket No.: DEX-0180  
Inventors: Roberto A. Macina  
Serial No.: 09/806,302  
Filing Date: July 19, 2001  
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**REMARKS**

Claims 1 and 11-21 are pending in the instant application. Claims 1, 11, 12, 15, 18 and 21 have been rejected. Claims 13, 14, 16, 17, 19 and 20 have been objected to. Reconsideration is respectfully requested in light of the following remarks.

The rejection of claims 1, 11, 12, 15, 18 and 21 under 35 U.S.C. 103(a) as being unpatentable over Lehrer (U.S. Patent Application No. 2002/0034739) in view of either Ni (U.S. Patent 6,066,724) or Gentz (WO 97/34997) has been maintained. The Examiner suggests that since the claimed methods include measurements in bodily fluids, they read on detection of metastasis of uterine or ovarian cancer. The Examiner suggests that Lehrer teaches methods for the detection of the metastasis of cancers and specifically points to cancers such as uterine or ovarian cancers (see paragraph 0011). The Examiner also suggests that Lehrer teaches the bone marrow or blood cells fail to express the genes for lipophilins and points out that the presence of lipophilins or the associated mRNA in the bloodstream is evidence for blood-borne dissemination of carcinoma cells originating from these organs (paragraph 0011). Further, the Examiner suggests that Lehrer teaches a comparison step because the measured levels in the blood would have to be compared to a normal control.

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Applicant respectfully traverses this rejection.

MPEP 2141.02 is clear; ascertaining the differences between the prior art and the claims at issue requires interpreting the claim language, and considering the invention and the prior art references as a whole (emphasis added). A prior art reference must be considered in its entirety, i.e. as a whole, including portions that would lead away from the claimed invention. See MPEP 2141.02 and W.L. Gore & Associates, Inc. v. Garlock, Inc. 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983) cert. denied, 469 U.S. 851 (1984). Thus, in accordance with MPEP 2141.02 the Examiner must consider the Lehrer reference in its entirety including the fact that all data presented in the published patent application relating to expression levels in cancer tissues teach away from the claimed invention.

Further, in accordance with MPEP 2143.01, where the teachings of a prior art reference conflict, the Examiner must weigh the suggestive power of each teaching.

In paragraph 0011, Lehrer is making a broad statement regarding the general utility of lipophilins based on the fact that low levels of native expression are observed in white blood cells and bone marrow tissue. See Figure 11A and 11B of Lehrer. Native expression in bone marrow or white blood cells is a confounding factor for designing a cancer diagnostic. Blood-based native expression is

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particularly problematic in diagnostic assays based upon detection of a gene, particularly a down-regulated gene, in blood. It is well known that if there is blood-based native expression, it will obscure changes associated with gene products shed by other normal tissue cells or cancerous cells.

However, while paragraph 0011 provides a general well known statement of how a diagnostic assay for metastases may be developed by detecting increased expression in blood of some markers, the only data presented by Lehrer relating to prostate cancer does not support utility of lipophilin C in such an assay. Specifically, Lehrer teaches that "lipophilin C is produced in prostatic cancer cell lines at levels lower than those characterizing normal prostate."

[Emphasis added] See paragraph [0047]. Lehrer goes on to teach that "prostate cancer cell lines and xenografts also show reduced expression of lipophilin B and lipophilin C."

[Emphasis added] See paragraph [0047]. Thus, the expectation based upon teachings of Lehrer is that one would detect a decrease in expression of lipophilin C in individuals with metastatic prostate cancer since the circulating prostate cancer cells express less lipophilin C than normal circulating prostate cells. Such data clearly has more suggestive power and thus outweighs the broad

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general statements regarding diagnostic assay development for metastatic cancer in paragraph 0011 of Lehrer.

Such data and the discussion set forth in paragraph 0047 of Lehrer also teaches away from the instant claimed invention, namely a method for detecting cancer wherein an increase in expression of ESBPIII is indicative of the cancer.

Claims of the instant application specifically describe a method for detecting the presence of uterine or ovarian cancer in a patient wherein an increase in measured levels of ESBPIII in the patient versus normal human control is associated with the presence of uterine or ovarian cancer. In contrast, the only expression data presented in Lehrer relates to experiments showing down regulation in prostate cancer cell lines and prostate cancer xenografts. Thus, Lehrer provides neither a reasonable expectation of success nor a convincing teaching or suggestion of all the claim limitations as required in accordance with MPEP 2143 to render the instant claimed invention obvious.

Given the fundamental shortcomings of the cited primary reference, Lehrer, any combination with the secondary references Ni and/or Gentz cannot make the claimed invention obvious. As stated in MPEP 2145, "it is

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improper to combine references where the references teach away from the combination."

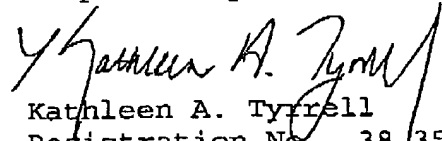
Withdrawal of this rejection under 35 U.S.C. 103(a) is therefore respectfully requested.

Claims 13, 14, 16, 17, 19 and 20 have been objected to as depending from a rejected claims. Since arguments presented above are believed to overcome this rejection of the claims from which claims 13, 14, 16, 17, 19 and 20, withdrawal of this objection is also respectfully requested.

#### Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

  
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